REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. Claims 30-34, 73, and 74 are currently pending and under consideration.

Withdrawal of Previous Bases of Rejection

Applicants acknowledge the Examiner's withdrawal of all previously outstanding bases of rejection, including the rejections under 35 U.S.C. §§ 103 and 112, second paragraph, as well as the double patenting rejection, in light of Applicant's arguments, the Declaration of Gaur, and the Terminal Disclaimer filed September 27, 2004.

Double Patenting Rejection

Claims 30-34, 73, and 74 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over U.S. Patent Nos. 6,369,033 (claims 1-10), 6,489,299 (claims 1-4), and 6,740,638 (claims 1-4) in view of Nishimoto *et al.* Although the reason underlying this basis of rejection is somewhat unclear, as the Examiner refers to U.S. Patent No. 6,329,499 rather than the instant application, it appears that the Examiner is asserting that claims drawn to MBP peptide analogs having a substituted residue 91, and including substitutions of N- and/or C-terminal residues with D-amino acids, for pharmaceutical purposes, are obvious in light of Nishimoto *et al.*'s teaching that a replacement of an L-amino acid residue with the corresponding D-isomer is a standard way of rendering the polypeptide less sensitive to proteolysis.

Applicants respectfully traverse this basis of rejection and submit that the instant claims are not obvious in light of the combination of any of the cited patents in view of Nishimoto *et al.* In particular, Applicants submit that it is not necessarily the case that the skilled artisan would desire a peptide analog to have increased stability. Rather, it is only the teachings of the instant specification that emphasize advantages associated with increased stability of the claimed peptide analogs.

Nonetheless, solely to expedite prosecution of the instant application and without acquiescence to this basis of rejection, Applicants submit herewith a Terminal Disclaimer directed to U.S. Patent Nos. 6,369,033, 6,489,299, and 6,740,638. Accordingly, Applicants respectfully request that this basis of rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 30-34, 73, and 74 stand rejected under 35 U.S.C. § 103, as allegedly obvious over Martin *et al.* in view of Nishimoto *et al.* More specifically, the Examiner asserts that Martin *et al.* teaches solid phase synthesized peptides comprising residues 88-100 of human myelin basic protein (MBP) with the lysine at residue 91 altered to an Ala. The Examiner further asserts that, due to numbering differences, these residues correspond to residues 87-99 of the human MBP referred to by Applicants. Presumably, Nishimoto *et al.* is asserted to teach and motivate the substitution of N- and/or C-terminal residues with D-amino acids.

Applicants respectfully traverse this basis of rejection and submit that the Examiner fails to establish a *prima facie* case of obviousness in light of the combination of Martin *et al.* and Nishimoto *et al.* More specifically, the Examiner fails to demonstrate that the combination of these references teaches or suggests each element of the claimed invention and fails to establish any motivation to combine the cited references to achieve the claimed invention. As established by the courts and enunciated in the M.P.E.P., "[o]bviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention when there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art." M.P.E.P., 8th Ed. § 2143.01.

As an initial matter, Applicants submit that the cited combination of references fails to teach each element of the claimed invention. Applicants note that the presently claimed peptide analogues comprise residues 86 to 99 of human myelin basic protein, whereas the peptide described by Martin *et al.* and referred to by the Examiner consists of residues 87-99. Therefore, the claimed peptides include residue 86, whereas the peptides described by Martin *et al.* do not include residue 86. Accordingly, since neither Martin *et al.* nor Nishimoto *et al.* teach

or suggest a peptide comprising the same residues of MBP as the claimed peptide analogues, Applicants submit that the combination of Martin *et al.* and Nishimoto *et al.* fails to teach each element of the claimed invention and, therefore, do not render the claimed invention obvious.

In addition, Applicants submit that neither Martin *et al.* nor Nishimoto *et al.* provide motivation for the skilled artisan to modify the teachings of Martin *et al.* to produce the claimed peptide analogues. Instead, Applicants submit that the teachings of Martin *et al.* would discourage the skilled artisan from making any such alterations to the peptides described therein. Martin *et al.* teaches that the $CD4^+$ cytotoxic T cell response to the human MBP immunodominant region that includes residues 86-105 (according to Applicants' numbering) demonstrates a high degree of heterogeneity at the level of fine specificity and TCR usage, suggesting that this region of human MBP contains overlapping and nested immunogenic epitopes. While Martin *et al.* demonstrates that a peptide corresponding to residues 87-99 and having an alanine substitution at residue 91 (Ala5) is capable of inducing a certain amount of TCL-mediated cell lysis (Figure 3), nowhere does Martin *et al.* demonstrate that a peptide corresponding to residues 86-99 has a similar effect. In addition, Applicants note that the Ala5 peptide described by Martin *et al.* promotes substantially less lysis than either the wild-type MBP peptide or several other alanine mutants, including, *e.g.*, Ala 9 and Ala 12 (Figure 3). Accordingly, the skilled artisan, apprised of these teachings of Martin *et al.*, would have no motivation to select a peptide containing an alanine mutation at position 91, since this substitution resulted in an inferior immune response as compared to other substitutions. Accordingly, Applicants submit that neither Martin *et al.* nor Nishimoto *et al.* provide motivation to alter the teachings of Martin *et al.* by adding an additional amino acid residue to the Ala5 peptide described therein, and, therefore, this combination of references fails to render the claimed invention obvious.

In addition, even assuming *arguendo* that Martin *et al.* taught a peptide comprising residues 86-99 and having an alanine substitution at residue 91, Applicants further submit that neither reference would motivate the skilled artisan to produce a claimed MBP peptide analogue wherein the N- and/or C-terminal residue is altered to a D-amino acid, since the understanding in the art was that substitutions from L- to D-isomers could not be assumed

beneficial, as acknowledged by the Examiner in the Office Action mailed December 2, 2003 (page 5, lines 1-5). Indeed, the Examiner himself points to references that teach that substitution of L- to D-isomers may not be beneficial for the inhibitory effect of a peptide analog, and, on the contrary, it may actually abolish the inhibitory effect (Teitelbaum *et al., Proc. Natl. Acad. Sci. USA* 85:9724-9728 (1988)). Accordingly, Applicants submit that the requisite motivation to alter an MBP peptide by substituting the N- and/or C-terminal residue with a D-amino acid did not exist, even in light of Nishimoto *et al.*, given the acknowledged understanding in the art that such substitutions may not be beneficial.

Applicants respectfully submit that the presently claimed invention is not obvious in light of the combination of Martin *et al.* and Nishimoto *et al.*, since neither reference teaches a peptide analogue comprising residues 86-99 of MBP, and neither reference would motive the skilled artisan to alter the peptides taught by Martin *et al.* to include residue 86 and a D-amino acid substitution, as recited. Applicants respectfully request that this basis of rejection be reconsider and withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims remaining in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Carol D. Laherty, Ph.D.
Registration No. 51,909

CDL:jto

Enclosure:
Postcard
Terminal Disclaimer

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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